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10/519,386	12/27/2004	Marie-Noelle Horcajada	P70350US0	6940

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EXAMINER	
JAVANMARD, SAHAR	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,386	HORCAJADA ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *17 May, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the 371 of PCT/FR03/02005 filed December 12, 2004. Amended claims 1-20 are being examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 5, 7, 15, 16, and 18 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment of disorders linked to an imbalance in the relationship between bone formation and bone resorption including a disease selected from osteoporosis, Paget's disease, bone loss or the osteolysis observed close to a prosthesis, metastatic bone diseases, the hypercalcemia due to a cancer, multiple myelomas, periodontal diseases or osteoarthritis disclosed in the specification, does not reasonably provide enablement for the prevention of the imbalance in the relationship between bone formation and bone resorption of the disorders recited in these claims.

The instant claims are drawn to a composition for the prevention of one or more symptoms of diseases or disorders associated with the imbalance in the relationship between bone formation and bone resorption of the disorders. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is

directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention pertains to a composition for the prevention of one or more symptoms of diseases or disorders associated with the imbalance in the relationship between bone formation and bone resorption of the disorders.

The state of the prior art:

One of ordinary skill in the art would appreciate that the prevention of one or more symptoms of diseases or disorders associated with the imbalance in the relationship between bone formation and bone resorption totally, absolutely, or permanently, is highly unlikely, since it is impossible to totally prevent disorders linked to an imbalance in the relationship between bone formation and bone resorption.

The relative skill of those in the art:

The relative skill of those in the art is very high.

The predictability or lack thereof in the art:

The ordinary artisan would view that the prevention of one or more symptoms of diseases or disorders associated with the imbalance in the relationship between bone formation and bone resorption, absolutely, or permanently is highly unpredictable, and since no one can guarantee that the diseases will be totally prevented.

The amount of direction or guidance presented and the presence or absence of working examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent one or more symptoms of diseases or disorders associated with the imbalance in the relationship between bone formation and bone resorption totally, absolutely, or permanently. Note that the lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether preventing one or more symptoms of diseases or disorders associated with the imbalance in the relationship between

bone formation and bone resorption totally, absolutely, or permanently, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation, "a derivative" in these claims renders claims indefinite. The recitation, "a derivative" is not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "a derivative" of compounds herein. As a result, any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. Thus, it is unclear as to what "a derivative" of compounds herein would be encompassed thereby.

Claims 1-11 and 13-20 provide for the “use of” the compound hesperidin or of one of its derivatives for the manufacture of a composition designed to stimulate bone formation and/or inhibit bone resorption in man or animals, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

As such, the claims are being treated as product claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-11 and 13-20 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-9 and 11-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Wenzel et al. (EP 1127572A2).

Wenzel teaches compositions of flavone-type compounds of formula I are useful in the treatment of cyclooxygenase-2 (COX-2) and nuclear factor kappa B (NF-κB) mediated diseases (page 2, lines 23-24).

COX-2 mediated diseases encompass acute exuditive inflammation, proliferative inflammation, animal arthritis, rheumatoid arthritis, angiogenesis, bone absorption, gastric ulcer, colon cancer, hyperalgesia, Alzheimer's disease, and certain states of the kidney, brain, and female reproductive organs (Katori, et al., Inflamm. Res., 49, 2000, p 367-392, abstract).

NF-κB mediated diseases include postmenopausal osteoporosis, rheumatoid arthritis, Paget's disease, periodontal disease, benign and malignant bone tumors, bone metastases, and hypercalcemia of malignancy (Hofbauer et al, J. Mol. Med., 79, 2001, p 243-253, abstract).

Thus the limitations of claim 1 are met.

In addition, Wenzel teaches, compositions of the compounds of formula I may be used as dietary supplements, added as the active ingredient to foods or medical foods or as oral compositions to treat COX-2 and NF-κB mediated diseases (page 8, lines 33-37; page 11, example 1; page 12, examples 5 and 6), meeting the limitations of claims 2 and 12.

Further, by definition, bone is hard tissue that is in a constant state of flux, being built up by bone-forming cells called osteoblasts while also being broken down or resorbed by cells known as osteoclasts. Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially of the hip, spine, and wrist. Osteoporosis occurs primarily as a result of normal ageing, but can arise as a result of impaired development of peak bone mass (e.g. due to delayed puberty or undernutrition) or excessive bone loss during adulthood (e.g. due to estrogen deficiency in women, undernutrition, or corticosteroid use) (defined by the World Health Organization). Thus the limitations of claims 4, 5, 6, and 7 are also met.

The reference teaches the compounds of formula I can be added to nutritional substances which can be a food preparation or an essential nutrient preparation. Food preparations particularly well suited include breakfast foods, such as prepared cereals, toaster

pastries, and breakfast drink mixes; infant formulas; dietary supplements; complete diet formulas; and weight-loss preparations, such as weight-loss drinks and weight-loss bars (page 10, lines 50-52; page 11, example 1; page 12, example 6), meeting the limitations of claims 3 and 8.

Furthermore, in example 6, an infant formula containing the flavone is administered, thus meeting a drink in wet form, meeting the limitations of claim 9.

Wenzel teaches the daily quantity of compounds of formula I by oral administration is between 10 mg to 700 mg (page 11 and 12, examples), meeting the limitations of claim 11.

Wenzel teaches the pharmaceutical compositions of formula I for the treatment of COX-2 and NF-κB mediated diseases to humans and other animals administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, or drops), bucally, or as an oral or nasal spray (page 8, lines 1-4), meeting the limitations of claims 13-19.

Further, Wenzel teaches that the total daily dose of the compounds of formula I administered to a human in single or in divided doses can be in amounts, for example, from 0.05 to about 500 mg/kg body weight daily or more preferably from about 1 to about 150 mg/kg body weight for oral administration or 0.01 to about 10 mg/kg for parenteral administration daily (page 12, lines 37-40), meeting the limitations of claim 20.

Claims 1-7, 9-10, and 12-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kise et al. (JP 2001114675A, enclosed is a machine translation that is being relied upon).

Kise teaches a vitamin composition containing vitamin K and flavonoids, including hesperidin or hesperitin (claims 1 and 3). Further, the reference teaches that the hesperidin is an extract of the fruit juice of citrus fruits (claim 7). The reference further teaches that compositions of vitamin K, vitamin D3, estrogen, isoflavone, etc., are known to prevent and treat

osteoporosis (page 2, [0003]). Kise also teaches that the composition can be in a soft capsule (page 5, [022]), meeting the limitations of claims 1-7, 9-10, and 12-19.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wenzel et al. (EP 1127572A2) in view of Barnes et al. (US Patent No. 5,506,211).

Wenzel is discussed above.

Wenzel does not teach the nutritional composition of hesperidin or one of its derivatives in the form of animal feed in a wet, semi-wet, or dry form.

Barnes teaches genistein, which is used to provide a method of use in inhibiting osteoclast activity to reduce bone loss (ie, in patients with osteoporosis), may be present in a variety of foodstuffs, particularly soy products, and may be ingested by animals to provide them with an effective amount genistein (column 3, lines 5-10).

Thus, it would have been obvious to one of ordinary skill in the art to have combined the methods of use of hesperidin as taught by Wenzel and used it in foodstuffs to be ingested by animals as taught by Barnes. Humans and animals can suffer from the same ailments; therefore, one would be motivated to use the same methods of treatment in animals as in humans.

Conclusion

Claims 1-20 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY STUCKER can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

SJ

JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER